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| 10/590,810 | 01/17/2007 | Jean-Luc Jestin | 295295US0X PCT | 2182 |

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| EXAMINER | |
|---|---|
| HUTSON, RICHARD G | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | |

| NOTIFICATION DATE | DELIVERY MODE |
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| 07/16/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/590,810 | JESTIN ET AL. | |
| | Examiner | Art Unit | |
| | Richard G. Hutson | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *4/30/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *7-9,11,13 and 19-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,12,14-18,65 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's preliminary amendment of claims 1, 15, 19, 24, 30, 45, 48, 51 and 55-64, in the paper of 7/3/2007, is acknowledged. Claims 1-66 are still at issue and are present for examination.

### *Election/Restrictions*

Applicant's election with traverse of Group I, Claims 1-18, 65 and 66, to a polynucleotide and (1) polynucleotide sequences encoding for polypeptides having 80% identity to residues 13-555 of SEQ ID No:26, wherein said polypeptide has at least one mutation, at position W550 (position 827 of the Taq polymerase wild-type); and (1) polynucleotide SEQ ID No:21 (at least claims 1-6, 10, 12, 14-18, 65 and 66 readable thereon). Applicants submit that the examiner has not provided any indication that the contents of the claims were considered in making the assertion of a lack of unity and therefore the examiner's burden has not been met. Applicant's complete argument is acknowledged and has been carefully considered, but is not found persuasive on the following basis.

As previously stated, the inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical

features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Barnes et al. (U.S. Patent No. 6,214,557, 2001) teach a purified polynucleotide which encodes a polypeptide comprising an amino acid sequence having at least 80% identity to residues 13-555 of SEQ ID NO:26, wherein the polypeptide has at least one mutation in amino acids 461-490 of SEQ ID NO: 26 or at a position selected from the group consisting of H203, F205, T232, E253, Q257, D274, L275, I276, V309, I322, A331, L332, D333, Y334, $335, I361, R374, A384, T387, Y419, P493, M498, G499, M502, L503, V506, R518, A523, A526, P539, E543, and W550, and wherein said polypeptide has DNA polymerase activity (See ISR and reference). Thus, the shared technical feature of the groups is not a “special technical feature”, unity of invention between the groups does not exist and thus the groups are subject to restriction as indicated previously. Upon determination of an allowable product, consideration will be given to those claims which are drawn to the use of said product.

Claims 7-9, 11, 13, 19-64 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the

list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure statement, filed 11/27/2006, is acknowledged. Those references considered have been initialed.

***Specification***

The disclosure is objected to because of the following informalities: Figure 6a, b and Figure 7 contain amino and or nucleic acied sequences which require a sequence identifier either in the Figure or its description.

**2422.02** The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures

37 CFR 1.821(b) requires exclusive conformance, with regard to the manner in which the nucleotide and/or amino acid sequences are presented and described, with the sequence rules for all applications that include nucleotide and amino acid sequences that fall within the definitions. This requirement is necessary to minimize any confusion that could result if more than one format for representing sequence data was employed in a given application. It is also expected that the required standard format will be more readily and widely accepted and adopted if its use is exclusive, as well as mandatory. In view of the fact that many significant sequence characteristics may only be demonstrated by a figure, the exclusive conformance requirement of this section may be relaxed for drawing figures. This is especially true in view of the fact that the representation of double stranded nucleotides is not permitted in the “Sequence Listing” and many significant nucleotide features, such as “sticky ends” and the like, will only be shown effectively by reference to a drawing figure. Further, the similarity or homology between/among sequences can only be depicted in an effective manner in a drawing figure. Similarly, drawing figures are recommended for use with amino acid sequences to depict structural features of the corresponding protein, such as finger regions and

Kringle regions. The situations discussed herein are given by way of example only and there may be many other reasons for relaxing the requirements of this section for the drawing figures. It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 65 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 65 is indefinite in the recitation "An insert contained in a phage selected from the group consisting of I-3168, 1-3169, 1-3170, 1-3171, 1-3172, 1-3173, 1-3174, 1-3175, 1-3176 and 1-3158 in CNCM on February 27, 2004." Because it is unclear as to exactly what it is that applicants are claiming. If it is applicants intent to claim a polynucleotide insert contained in a phage that has been deposited at an approved depository, applicants are requested to amend the claim to specifically reflect this. In order to advance prosecution this is how this claim is interpreted.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 10, 12, 14-18, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6, 10, 12, 14-18, 65 and 66 are directed to all possible polynucleotides which encodes a thermostabte polypeptide comprising an amino acid sequence having at least 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides encoding mutant polymerases by any identifying structural characteristics or properties, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-6, 10, 12, 14-18, 65 and 66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for that polynucleotide encoding a thermostable polypeptide, wherein said polynucleotide comprises the nucleic acid sequence of SEQ ID NO:21, does not reasonably provide enablement for any polynucleotide which encodes a thermostabte polypeptide comprising an amino acid sequence having a mere 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-6, 10, 12, 14-18, 65 and 66 are so broad as to encompass any polynucleotides which encodes a thermostabte polypeptide comprising an amino acid sequence having a mere 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims, including all homologues, a modified forms, a functional equivalents or an effective fragments thereof any polynucleotides which encodes a thermostabte polypeptide comprising an amino acid sequence having at least 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity. The claims rejected under this section of U.S.C. 112, first paragraph, place minimal if any structural limits on the claimed polynucleotides and referenced polymerase polypeptides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that that polynucleotide comprising the nucleic acid sequence of SEQ ID NO:21.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any polynucleotide which encodes a thermostabte polypeptide comprising an amino acid sequence having at least 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase activity; (B) the general tolerance of polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a polymerase encoding polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the polymerase activity claimed and the fact that the relationship between the sequence

of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus encoding a polypeptide with the claimed polymerase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any polynucleotides which encodes a thermostabte polypeptide comprising an amino acid sequence having at least 80% identity to residues 13-555 of SEQ ID NO: 26, wherein said polypeptide has at least one mutation at a position W550, and wherein said polypeptide has DNA polymerase activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

As is noted above under rejection under 112 second paragraph, claim 65 recites an insert contained in a phage selected from the group consisting of I-3168, 1-3169, 1-3170, 1-3171, 1-3172, 1-3173, 1-3174, 1-3175, 1-3176 and 1-3158 in CNCM on

February 27, 2004. To the extent that this deposited accession number is necessary to enable the claim currently or after applicant's amendment, claim 65 is further rejected as not being enabled on the following basis.

Claim 65 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claim 65 appears to employ a novel strain of phage(s). Since the phage is essential to the claimed "insert" (See above rejection under 112 second paragraph), it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The organism is not fully disclosed, nor has it been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the bacterium. under the Budapest treaty and an indication as to public availability. An affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

***Remarks***

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mondesi Robert can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
7/9/2010

/Richard G Hutson/
Primary Examiner, Art Unit 1652